Does povidone-iodine application in surgical procedures help in the prevention of surgical site infections? An updated meta-analysis

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Abstract

Introduction: *Surgical site infections (SSIs) occur after an operative procedure and can range from superficial to deep wound infections. The World Health Organization (WHO) and the Centers for Disease Control (CDC) have proposed guidelines recommending measures to prevent SSIs. Intraoperative measures are largely focused on decontamination of the skin and intraoperative wound irrigation using soap and antiseptics and are simple, efficient, and cost-effective measures to reduce SSIs. Povidone-iodine (PVI) is a topical antiseptic widely used for the reduction of SSIs.*
Aim: *A meta-analysis was conducted to determine the efficacy of preoperative or intraoperative use of PVI from randomized controlled trials (RCTs).*
Material and methods: *A systematic literature review was conducted using MEDLINE and Central databases for RCTs that involved PVI application versus saline or no treatment control groups across various surgical categories. The primary outcome was SSI or post-operative wound infections. A random-effects model was used to calculate the pooled risk ratio and subgroup analyses were performed.*
Results: *A total of 59 RCTs were included in the meta-analysis with information from 20,497 patients. A reduction in overall SSI incidence was found (RR = 0.70, 0.60–0.80, p = 0.0002,* I^2 *= 44%). Subgroup analyses showed that the comparator treatment and type of procedure did not modify the effect of PVI on SSI incidence. However, inconsistent results on SSI incidence were obtained when the data were stratified by PVI application method and surgery category.*
Conclusions: *The results of the meta-analysis provide support for the preoperative or intraoperative use of PVI in decreasing the incidence of SSI.*

Key words: *povidone iodine, surgical site infections, skin preparation, wound irrigation, normal saline.*

Introduction

Surgical site infections (SSIs) occur after an operative procedure and can range from superficial to deep wound infections. Global estimates of SSIs have ranged from 0.5% to 15%, whereas studies in India have consistently shown higher rates from 23% to 38% [1]. SSIs are a substantial cause of morbidity, prolonged hospitalization, hospital readmissions, and death and pose a considerable financial burden on healthcare systems [2, 3]. Thus, prevention and minimization of SSIs improve patient outcomes and reduce resource consumption [4, 5].

Strategies to reduce the risk of SSIs include interventions that can be delivered preoperative-

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ly, intraoperatively, or postoperatively. The World Health Organization (WHO) and the Centers for Disease Control (CDC) have proposed guidelines recommending measures to prevent SSIs [6–8]. Sterile procedures, maintaining patient homeostasis, wound closure interventions, and prophylactic antibiotics are commonly used to reduce SSI risk [9]. Intraoperative measures primarily focus on decontamination of the skin and intraoperative wound irrigation using soap and antiseptics and are a simple, efficient, and cost-effective measure to reduce SSIs [10]. The most frequently used antiseptic is povidone-iodine (PVI), commonly applied as irrigation or a spray. PVI is an iodophor in which iodine is complexed with the polymer povidone. The microbicidal activity of iodine involves inhibition of vital bacterial cellular mechanisms and structures [11].

In contrast to antibiotics, antiseptics have a broader spectrum of activity and a reduced likelihood of resistance. However, despite the potential usefulness of topical antiseptics, current clinical practice is variable and largely dependent on surgeon preference. Furthermore, the routine use of topical antibiotics and antiseptics has been associated with adverse effects such as tissue toxicity and interference with wound healing [12, 13].

Although systematic reviews and meta-analyses on the benefits of PVI in reducing the incidence of SSIs have been published, there has been no definite conclusion on the effectiveness of PVI in different surgical categories [10, 14–16].

Aim

The objective of this paper is to synthesize current evidence from available randomized controlled trials evaluating the efficacy of PVI vs. saline/no treatment controls in decreasing the incidence of SSI.

Material and methods

The meta-analysis was carried out using the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines. We followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) normative recommendations in this study with the registration number LPH#/IRB/2021/1025.

Informed consent was not taken because of meta-analysis nature of this study.

Search strategy

A systematic literature search was conducted of MEDLINE (PubMed) and Cochrane Register of Controlled Trials (CENTRAL) in June 2021. No time limit was applied as several studies were published earlier than 1990. The following search terms were used in various combinations: surgical site infection, wound infection, SSI, post-operative, povidone-iodine, betadine, irrigation, and spray, and lavage, intraoperative and anti-infective agents. Additionally, a comprehensive list of search terms, including Medical Subject Headings (MeSH) terms, was applied. The titles and abstracts of potentially relevant studies were scanned, and the full-text versions of the relevant articles were read. Additional studies were identified by cross-checking the reference lists of the relevant studies.

Study selection or inclusion/exclusion criteria

Randomized controlled studies (RCTs) and prospective randomized studies that compared povidone-iodine application in any form (irrigation, spray, lavage, scrub) either preoperatively or intraoperatively were included across various surgical categories. The comparator treatment in the studies was primarily saline or no treatment. All studies reporting SSIs or wound infections as outcomes were included irrespective of the definition of SSI used. Exclusion criteria were non-randomized studies, animal studies, and studies with bacteriological counts as endpoints.

Data extraction and quality assessment

Following identification of articles that met the inclusion criteria, data were extracted using a predefined data extraction form that included the following items: study author, publication year, surgery category, inclusion criteria, intervention, control, SSI data in each group, PVI administration method, follow-up time, type of procedure, any systemic or prophylactic antibiotic use and other comments (if necessary).

The Cochrane Collaboration's risk of bias tool was used to assess the methodological quality of the included studies [17]. This tool includes the following criteria: randomization, allocation concealment, blinding, and completeness of follow-up. In addition, the risk of bias for each item was graded as high, low, or unclear risk.

Statement of ethics

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Helsinki Declaration and its later amendments or comparable standards. Informed consent was not required due to the meta-analysis nature of this study. This study was approved by the Research Ethics Committee of Liyang People's Hospital with the registration number of LPH#/IRB/2021/1025.

Quantitative data synthesis

Meta-analysis was performed using Review Manager (RevMan, Version 5. Copenhagen: The Nordic Cochrane Center, the Cochrane Collaboration. 2020). Absolute numbers of participants in each study developing a wound infection or SSI and the total number of participants in each group (intervention and control group) were used to calculate the risk ratio and the 95% confidence interval (CI). Meta-analyses were done using a random-effects model (Mantel-Haenszel method), and heterogeneity in the included studies was evaluated using the I^2 statistic, with small heterogeneity for I^2 values of 25%, moderate heterogeneity for I^2 values of 25% to 50%, and high heterogeneity for I^2 values > 50% [18]. Forest plots were constructed, and $p < 0.05$ was statistically significant. Subgroup analyses were also performed according to the type of comparator, PVI administration method, surgery category, and type of procedure.

Publication bias was assessed by a funnel plot in which the log risk ratio for each study was plotted against its standard error. Egger's and Begg's tests were performed using Comprehensive Meta-Analysis (Version 3.3.070) [19].

Results

Identification of studies

A total of 1976 records were identified by database searching, of which 1856 were screened by title and abstract. Duplicates and irrelevant records were removed (n = 1758), and 98 RCTs were assessed for eligibility. However, 39 RCTs were excluded due to reasons such as inappropriate comparator (other antiseptic or PVI of different concentrations), duplicate data, use of antiseptics other than PVI, or absence of information on SSI or wound infection as an outcome. The process of selection is shown in Figure 1.

Study characteristics

Fifty-nine RCTs totaling 20,497 participants met the inclusion criteria (PVI intervention group: 10148 participants and control group: 10349 participants). These RCTs involved the comparison of PVI intervention to saline or no treatment control groups across various surgical categories. All studies were randomized controlled trials or prospective randomized studies with sample sizes ranging from 29 to 3027. The studies included male and female participants undergoing various elective and urgent surgical procedures.

In 34 of the selected studies, PVI was administered as an irrigation solution, and it was given as a dry powder spray in 13 studies. The comparators in the studies were no treatment or propellant only and saline. The concentration of PVI ranged from 0.35% to 10%. Table I shows the characteristics of the intervention and control groups of the studies included for meta-analysis [20–78].

Characteristics of surgical interventions

Most studies were conducted in participants undergoing abdominal surgery (n = 26), gynecological procedures, specifically elective or urgent cesarean section (n = 17), and appendectomy (n = 8). Elective operations were performed in 25 studies, urgent operations in 12 studies, and mixed operations in 22 studies. The use of antibiotics was inconsistent between the studies but was administered in both

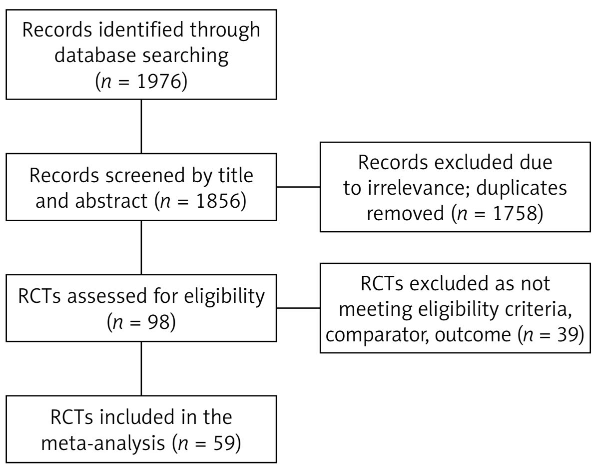

Figure 1. Flow chart for identification and inclusion of studies in the meta-analysis

Table I. Characteristics of intervention and control groups of the included studies

Reference	Intervention	Control	Type of PVI administration
Anderson 2020 [20]	PVI	None	Irrigation
Alobaidy 2020 [21]	PVI	None	Irrigation
Aref 2018 [22]	10% PVI solution	None	Irrigation
Asad 2017 [23]	PVI solution	None	Irrigation
Asghania 2011 [24]	10% PVI solution	None	Scrub
Barat 2016 [25]	10% PVI solution	None	Irrigation
Barr 1978 [26]	PVI	None	Lavage
Calkins 2019 [27]	Dilute Betadine and 10% Betadine	Saline	Lavage
Chang 2006 [28]	0.35% PVI + 2000 ml normal saline	2000 ml normal saline	Irrigation
Charoenviboonphan 2011 [29]	1% PVI paint	None	Paint
Cheng 2005 [30]	0.35% PVI + 2000 ml normal saline	Saline	Irrigation
Cohen 2020 [31]	0.35% PVI	Saline	Irrigation
de Jong 1982 [32]	1% and 10% PVI solution	None	Irrigation
Foster 1981 [33]	PVI dry powder	None	Spray
Galland 1977 [34]	PVI dry powder	None	Spray
Galland 1983 [35]	PVI aerosol	None	Spray
Galle 1980 [36]	PVI solution	Saline	Irrigation
Ghafouri 2016 [37]	1% PVI solution	Saline	Irrigation
Gilmore 1974 [38]	PVI dry powder	None	Spray
Gilmore 1975 [39]	PVI dry powder	Propellant alone	Spray
Gilmore 1977 [40]	PVI dry powder	Propellant alone	Spray
Gray 1981 [41]	PVI dry powder	None	Spray
Guzman 2002 [42]	PVI solution	Saline	Irrigation
Haas 2010 [43]	1% PVI solution	None	Scrub
Haider 2018 [44]	1% PVI solution	None	Irrigation
Harihara 2006 [45]	PVI solution	Saline	Irrigation
Hassan 2016 [46]	10% PVI solution	Saline	Irrigation
Iqbal 2015 [47]	1% PVI solution	None	Irrigation
Johnson 1985 [48]	50 ml of 1% PVI	Saline	Irrigation
Karuserci 2019 [49]	10% PVI + saline	Saline	Irrigation
Ko 1992 [50]	0.5% PVI solution in saline	Saline	Irrigation
Kokavec 2008 [51]	0.35% PVI solution	Saline	Irrigation
Kothi 1981 [52]	PVI solution	None	Irrigation
Lau 1986 [53]	10 ml 1% PVI solution	None	Irrigation
Mahomed 2016 [54]	50 ml 10% PVI solution	None	Irrigation
Memon 2011 [55]	10% PVI	None	Scrub
McCluskey 1976 [56]	10% PVI solution	None	Irrigation

Table I. Cont.

Reference	Intervention	Control	Type of PVI administration
Morgan 1978 [57]	PVI spray	None	Spray
Naunton Morgan 1980 [58]	PVI dry powder	None	Spray
Muller 2018 [59]	1000 ml PVI solution	1000 ml Ringer's lactate solution	Irrigation
Mwangi 2013 [60]	PVI solution	None	Irrigation
Nandi 2015 [61]	PVI	None	Scrub
Oestreicher 1989 [62]	10% PVI solution	Saline	Irrigation
Olmez 2013 [63]	PVI solution	None	Irrigation
Parker 1985 [64]	10% PVI solution	Water	Lavage
Pollock 1978 [65]	PVI spray	Sterile saline	Spray
Reid 2001 [66]	10% PVI solution	None	Scrub
Rogers 1983 [67]	10% PVI solution	Normal saline	Irrigation
Sherlock 1984 [68]	PVI spray	None	Spray
Sindelar 1979a [69]	0.1% PVI solution	Saline	Irrigation
Sindelar 1979b [70]	10% PVI solution	Saline	Irrigation
Sindelar 1985 [71]	1% PVI solution	Saline	Irrigation
Starr 2005 [72]	5% PVI solution	None	Scrub
Stokes 1977 [73]	PVI spray	None	Spray
Vallance 1985 [74]	100 ml PVI + saline	Normal saline	Lavage
Vinay 2019 [75]	5% PVI solution	Normal saline	Irrigation
Walker 2013 [76]	10% PVI solution	Saline	Gauze soaked
Walsh 1981 [77]	0.5% Betadine spray	None	Spray
Yildirim 2012 [78]	PVI solution	None	Irrigation

intervention and control groups of the studies with prophylactic antibiotics (n = 21). Table II summarizes the characteristics of the surgical procedures and types of procedures included for quantitative synthesis.

Bias assessment

The results of the risk of bias evaluation are shown in Figure 2. Overall, there was a high risk of bias due to unclear or high risk related to selection and performance bias and unclear risks associated with detection and reporting bias.

The funnel plot was asymmetrical (Figure 3), and Egger's and Begg's tests were statistically significant, indicating the possibility of publication bias.

Surgical site or wound infection rates

The incidence of SSI or wound infection in the included studies is shown in Table III. The SSI incidences ranged from 0% to 84.6% in the PVI group and from 0.6% to 75% in the control group (no treatment or saline). The overall incidence of SSI was 6.6% in the PVI intervention group and 9.4% in the control group.

Meta-analysis results

The results of the meta-analysis for all the studies included (n = 59) showed a reduction in the incidence of SSI and wound infections with the application of PVI in any form across all surgical categories compared to saline treatment or no treatment controls, which was statistically significant (RR = 0.70, 0.60 to 0.80, p = 0.0002, I^2 = 44%) (Figure 4).

Stratification of the results by the type of comparator showed that the decrease in SSI incidence remained statistically significant for PVI vs. saline or no treatment control groups (Figure 5). The test for subgroup differences indicated no statistically sig-

Table II. Characteristics of included studies

Reference	Surgery type	Type of procedure (Urgent/elective)	Sample size	Follow-up
Anderson 2020 [20]	Abdominal	Urgent	100	1 year
Alobaidy 2020 [21]	Gynecological	Elective	400	NS
Aref 2018 [22]	Gynecological	Elective	207	NS
Asad 2017 [23]	Gynecological	Urgent	434	3 weeks
Asghania 2011 [24]	Gynecological	Elective	568	NS
Barat 2016 [25]	Gynecological	Elective	400	6 weeks
Barr 1978 [26]	Abdominal	Mixed	88	NS
Calkins 2019 [27]	Orthopedic	Elective	457	90 days
Chang 2006 [28]	Spinal	Elective	244	19 months
Charoenviboonphan 2011 [29]	Gynecological	Mixed	599	NS
Cheng 2005 [30]	Spinal	Elective	414	15.5 months
Cohen 2020 [31]	Spinal	Elective	153	30 days
de Jong 1982 [32]	Abdominal+mixed	Mixed	582	4 weeks
Foster 1981 [33]	Abdominal	Urgent	236	4 weeks
Galland 1977 [34]	Abdominal	Mixed	78	NS
Galland 1983 [35]	Abdominal	Urgent	200	4 weeks
Galle 1980 [36]	Abdominal		67	NS
Ghafouri 2016 [37]	Trauma	Urgent	389	NS
Gilmore 1974 [38]	Abdominal	Mixed	300	4 weeks
Gilmore 1975 [39]	Abdominal	Mixed	144	6 weeks
Gilmore 1977 [40]	Non-abdominal	Mixed	101	6 weeks
Gray 1981 [41]	Abdominal	Elective	153	2 weeks
Guzman 2002 [42]	Gynecological	Elective	160	NS
Haas 2010 [43]	Gynecological	Elective	300	1 month
Haider 2018 [44]	General	Elective	600	4 weeks
Harihara 2006 [45]	Gastric and colorectal	Elective	107	NS
Hassan 2016 [46]	Gynecological	Elective	100	NS
Iqbal 2015 [47]	Abdominal	Urgent	166	30 days
Johnson 1985 [48]	Proctectomy for carcinoma	Elective	56	3 months
Karuserci 2019 [49]	Abdominal	Mixed	200	30 days
Ko 1992 [50]	Cardiopulmonary bypass	Mixed	1980	30 days
Kokavec 2008 [51]	Orthopedic	Elective	162	1.5 month
Kothi 1981 [52]	Abdominal	Elective	220	2 weeks
Lau 1986 [53]	Abdominal	Urgent	315	6 weeks
Mahomed 2016 [54]	Gynecological	Elective and Urgent	3027	4 weeks
McCluskey 1976 [55]	Abdominal	Mixed	110	4 weeks
Memon 2011 [56]	Gynecological	Mixed	200	NS

Table II. Cont.

Reference	Surgery type	Type of procedure (Urgent/elective)	Sample size	Follow-up
Morgan 1978 [57]	Accident trauma	Urgent	320	6 days
Naunton Morgan 1980 [58]	Accident trauma	Urgent	572	NS
Muller 2018 [59]	Abdominal	Elective	44	30 days
Mwangi 2013 [60]	Gynecological	Mixed	397	2 weeks
Nandi 2015 [61]	Gynecological	Mixed	294	NS
Oestreicher 1989 [62]	Mixed	Mixed	540	NS
Olmez 2013 [63]	Gynecological	Mixed	667	NS
Parker 1985 [64]	Resection of bowel carcinoma	Elective	45	NS
Pollock 1978 [65]	Abdominal	Mixed	139	4 weeks
Reid 2001 [66]	Gynecological	Elective	430	NS
Rogers 1983 [67]	Abdominal+mixed	Mixed	187	4 weeks
Sherlock 1984 [68]	Abdominal	Urgent	75	4 weeks
Sindelar 1979a [69]	Abdominal	Elective	168	NS
Sindelar 1979b [70]	General	Mixed	500	12 weeks
Sindelar 1985 [71]	Abdominal	Mixed	75	NS
Starr 2005 [72]	Gynecological	Elective	308	NS
Stokes 1977 [73]	Abdominal	Urgent	117	NS
Vallance 1985 [74]	Abdominal	Mixed	29	1 month
Vinay 2019 [75]	Abdominal	Elective	180	30 days
Walker 2013 [76]	Vascular	Elective	67	6 weeks
Walsh 1981 [77]	Abdominal	Mixed	627	4 weeks
Yildirim 2012 [78]	Gynecological	Mixed	669	6 weeks

NS – not specified.

nificant subgroup effect (p = 0.63), suggesting that comparator type does not modify the effect of PVI. However, the heterogeneity was high (I^2 = 60%) in the saline comparator subgroup, suggesting inconsistency in the studies included.

Subgroup analysis by PVI application method showed that the decrease in SSI incidence was statistically significant when PVI was administered as irrigation or spray compared to saline or no treatment. However, PVI application as a lavage or scrub did not cause any significant decrease in SSI vs. control (Figure 6). Further, the test for subgroup analysis revealed no statistically significant subgroup effect (p = 0.38), suggesting that the PVI application method does not modify the effect of PVI. However, a smaller number of studies contributed to data in the lavage and scrub subgroups.

Subgroup analysis by surgery category showed inconsistent effects of PVI on SSI incidence. Statistically significant results were seen in abdominal, gynecological, spinal, and orthopedic procedures, whereas no statistically significant effects were seen in accident surgery (Figure 7). The test for subgroup differences was not statistically significant (p = 0.05). The heterogeneity statistic (I^2 value) and the number of studies in each subgroup were inconsistent.

Stratification by the type of procedure (elective, urgent, or mixed) showed a reduction in SSI incidence, which was statistically significant and which was consistent across all subgroups (Figure 8). The test for subgroup differences indicated no statistically significant subgroup effect (p = 0.94), suggesting that type of procedure does not modify the effect of PVI. Heterogeneity was low to moderate in the subgroups.

Figure 2. Risk of bias summary for studies included in the meta-analysis

Discussion

The present study provides current and valuable information on the usefulness and efficacy of PVI in decreasing SSI incidence across various surgical categories and procedures. This meta-analysis showed that topical application of PVI in the preoperative or intraoperative phase for the 59 RCTs resulted in a decreased incidence of SSI by 30%. This favorable effect was mainly observed for patients undergoing abdominal and gynecological (cesarean section) surgery with a 22% and 19% reduction in SSI incidence. The heterogeneity values were low to moderate for these surgical categories, providing confidence in the values of the pooled risk ratios. Although beneficial effects were also seen for orthopedic and spinal surgery, the number of studies was insufficient and the I^2 heterogeneity statistic high. The high heterogeneity values can be attributed to diverse patient characteristics as some studies were carried out in pediatric populations.

Significant and consistent benefits of PVI were also observed in elective, urgent, and mixed procedures, although the studies showed moderate heterogeneity. This heterogeneity can be attributed to the type of surgery performed and variable patient characteristics. The effects of PVI were not consistent depending upon the application method, although the subgroup effect was not significant. PVI administration as irrigation or spray resulted in a significant decrease in SSI incidence, whereas administration as a lavage or scrub did not provide significant benefit. However, the number of studies for the lavage and scrub groups was too small (n = 10 studies) to allow a definite conclusion to be made.

The type of comparator (saline or no treatment) does not modify the effect of PVI. However, studies carried out using either comparator showed a significant decrease in SSI when PVI was administered in any form compared to the control.

In only one study, Muller *et al.* [59], laparoscopic surgery was done in 78.3% of procedures in the PVI group and 81% of procedures in the control group. However, individual SSI incidences for the laparoscopic vs. conventional methods were not reported.

Although the current meta-analysis suggests that preoperative or intraoperative use of PVI is associated with an overall decrease in SSI compared to saline or no treatment, it is essential to understand

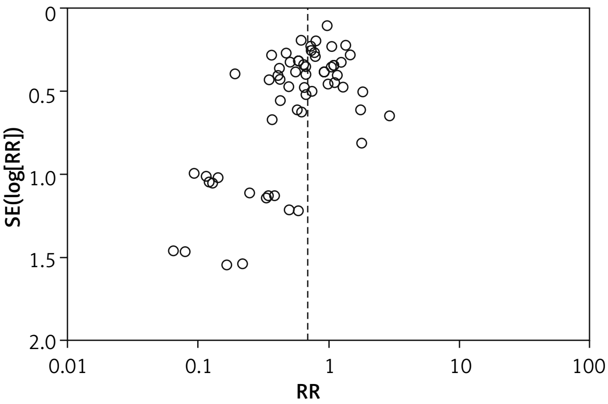

Figure 3. Funnel plot to assess publication bias in meta-analysis

the limitations of the studies included. Risk of bias analysis showed uncertain quality for most domains for the RCTs, indicating the possibility of selection, performance, and detection bias, raising concerns over the reliability of the studies. Adequate methods of allocation concealment and blinding were unclear in the studies, making it challenging to assess the trial quality. Additionally, prophylactic antibiotic administration and post-operative antibiotic use were not consistent between the RCTs. Preoperative antibiotics were administered to PVI and control groups in 28 studies without a relationship between SSI incidence and antibiotic use. Antibiotic use can significantly affect SSI rates and produce an inflated estimate of SSI reduction which may not be related to PVI treatment. Follow-up times for observation of SSI development differed between the studies. The current CDC definition for an SSI recommends a follow-up time of 30 days [8], whereas a few studies reported shorter time frames for post-surgery observation, which is an additional cause of variability for the outcome. Included studies were heterogeneous with regards to populations, prophylactic antibiotic use, and time of PVI application. Since several studies included in the meta-analysis were published before 1990 (n = 27), it is essential to consider possible changes in surgical practices that can modify the benefits of PVI.

Conclusions

Regardless of possible limitations, the present meta-analysis indicates that preoperative and intraoperative use of PVI is beneficial in decreasing SSI incidence. However, for surgeons to justify the use of PVI,

Table III. Surgical site infection (SSI) or wound infection incidences in the included studies

Reference	SSI incidence (%)	
	Intervention: PVI	Control: saline or no treatment
Anderson 2020 [20]	12	16
Alobaidy 2020 [21]	0.5	1
Aref 2018 [22]	3.8	5.9
Asad 2017 [23]	1.4	3.7
Asghania 2011 [24]	3.5	3.2
Barat 2016 [25]	6	6.5
Barr 1978 [26]	3.6	38.3
Calkins 2019 [27]	0.4	3.4
Chang 2006 [28]	0	4.8
Charoenviboonphan 2011 [29]	0.3	1.3
Cheng 2005 [30]	0	3.4
Cohen 2020 [31]	1.3	2.6
de Jong 1982 [32]	12.9	16.1
Foster 1981 [33]	24.4	23.1
Galland 1977 [34]	35.9	46.2
Galland 1983 [35]	13.7	13.3
Galle 1980 [36]	29	25
Ghafouri 2016 [37]	7.7	7.3
Gilmore 1974 [38]	8.1	15.9
Gilmore 1975 [39]	8.6	24.3
Gilmore 1977 [40]	0	3.8
Gray 1981 [41]	9.9	24.4
Guzman 2002 [42]	8.8	5
Haas 2010 [43]	4.5	6.9
Haider 2018 [44]	6.3	8
Harihara 2006 [45]	14.8	15.1
Hassan 2016 [46]	2	14
Iqbal 2015 [47]	10.8	19.3
Johnson 1985 [48]	35.7	75
Karuserci 2019 [49]	6	12
Ko 1992 [50]	1.1	0.6
Kokavec 2008 [51]	0	2.7
Kothi 1981 [52]	15.7	12.7
Lau 1986 [53]	5.7	1.9
Mahomed 2016 [54]	9.5	9.8
McCluskey 1976 [55]	37.5	25.9
Memon 2011 [56]	1	3
Morgan 1978 [57]	6	14.3
Naunton Morgan 1980 [58]	5.3	14.6
Muller 2018 [59]	17.4	9.5
Mwangi 2013 [60]	6.5	10.2
Nandi 2015 [61]	2.9	5.1
Oestreicher 1989 [62]	6	5.5
Olmez 2013 [63]	10.5	17
Parker 1985 [64]	4.5	39.1
Pollock 1978 [65]	26.2	35.1
Reid 2001 [66]	5.5	8.5
Rogers 1983 [67]	4.7	10.9
Sherlock 1984 [68]	15.4	36.1
Sindelar 1979a [69]	1.3	10.2
Sindelar 1979b [70]	2.9	15.1
Sindelar 1985 [71]	2.7	7.9
Starr 2005 [72]	0.7	1.2
Stokes 1977 [73]	20	33.9
Vallance 1985 [74]	84.6	62.5
Vinay 2019 [75]	10	7.8
Walker 2013 [76]	3.2	8.3
Walsh 1981 [77]	9.1	12.5
Yildirim 2012 [78]	1.8	2.7

its application must be carried out taking into consideration current surgical practices and procedures.

What is the 'take-home' message for the clinician?

Antisepsis of the surgery region and antibiotic prophylaxis are critical preoperative preventative treatments. In visceral surgery, intraoperative wound irrigation with povidone-iodine solution decreases SSI.The use of intra-operative PVI may help to lower SSI rates. Because there are few recent studies and surgical techniques may have changed, modern, properly powered, and well-designed clinical trials, stratified by antibiotic treatment and wound contamination, and using an up-

Study or subgroup	PVI		Control		Weight	Risk ratio M-H,
	Events	Total	Events	Total	(%)	random, 95% CI
Alobaidy 2020	1	200	2	200	0.3	0.50 (0.05–5.47)
Anderson 2020	6	50	8	50	1.5	0.75 (0.28, 2.00)
Aref 2018	4	106	6	101	1.1	0.64 (0.18, 2.19)
Asad 2017	3	217	8	217	1.0	0.38 (0.10, 1.39)
Asghania 2011	10	284	9	284	1.7	1.11 (0.46, 2.69)
Barat 2016	12	200	13	200	2.1	0.92 (0.43, 1.97)
Barr 1978	1	28	23	60	0.5	0.09 (0.01, 0.66)
Calkins 2019	1	223	8	234	0.4	0.13 (0.02, 1.04)
Chang 2006	0	120	6	124	0.2	0.08 (0.00, 1.40)
Charoenviboonphan 2011	1	299	4	300	0.4	0.25 (0.03, 2.23)
Cheng 2005	0	208	7	206	0.2	0.07 (0.00, 1.15)
Cohen 2020	1	77	2	76	0.3	0.49 (0.05, 5.33)
de Jong 1982	39	303	45	279	3.6	0.80 (0.54, 1.19)
Foster 1981	29	119	27	117	3.3	1.06 (0.67, 1.67)
Galland 1977	14	39	18	39	2.9	0.78 (0.45, 1.33)
Galland 1983	13	95	14	105	2.3	1.03 (0.51, 2.07)
Galle 1980	9	31	9	36	2.0	1.16 (0.53, 2.56)
Ghafouri 2016	15	196	14	193	2.3	1.06 (0.52, 2.13)
Gilmore 1974	12	149	24	151	2.5	0.51 (0.26, 0.98)
Gilmore 1975	6	70	18	74	1.8	0.35 (0.15, 0.84)
Gilmore 1977	0	48	2	53	0.2	0.22 (0.01, 4.48)
Gray 1981	7	71	20	82	2.0	0.40 (0.18, 0.90)
Guzman 2002	7	80	4	80	1.1	1.75 (0.53, 5.75)
Haas 2010	7	155	10	145	1.6	0.65 (0.26, 1.67)
Haider 2018	19	300	24	300	2.8	0.79 (0.44, 1.41)
Harihara 2006	8	54	8	53	1.7	0.98 (0.40, 2.42)
Hassan 2016	1	50	14	100	0.5	0.14 (0.02, 1.06)
Iqbal 2015	9	83	16	83	2.1	0.56 (0.26, 1.20)
Johnson 1985	10	28	21	28	2.9	0.48 (0.28, 0.82)
Karuserci 2019	6	100	12	100	1.6	0.50 (0.20, 1.28)
Ko 1992	11	990	6	990	1.5	1.83 (0.68, 4.94)
Kokavec 2008	0	89	2	73	0.2	0.16 (0.01, 3.37)
Kothi 1981	16	102	15	118	2.5	1.23 (0.64, 2.37)
Lau 1986	9	159	3	156	1.0	2.94 (0.81, 10.67)
Mahomed 2016	144	1520	147	1507	4.5	0.97 (0.78, 1.21)
McCluskey 1976	21	56	14	54	2.8	1.46 (0.82, 2.54)
Memon 2011	1	100	3	100	0.4	0.33 (0.04, 3.15)
Morgan 1978	10	166	22	154	2.2	0.42 (0.21, 0.86)
Naunton Morgan 1980	14	263	45	309	2.8	0.37 (0.21, 0.65)
Muller 2018	4	23	2	21	0.7	1.83 (0.37, 8.96)
Mwangi 2013	13	201	20	196	2.4	0.63 (0.32, 1 24)
Nandi 2015	4	136	7	138	1.1	0.58 (0.17, 1.94)
Oestreicher 1989	16	267	15	273	2.4	1.09 (0.55, 2.16)
Olmez 2013	35	332	57	335	3.6	0.62 (0.42, 0.92)
Parker 1985	1	22	9	23	0.5	0.12 (0.02, 0.84)
Pollock 1978	17	65	26	74	3.1	0.74 (0.45, 1.24)
Reid 2001	12	217	18	213	2.3	0.65 (0.32, 1.33)
Rogers 1983	4	86	11	101	1.3	0.43 (0.14, 1.29)
Sherlock 1984	6	39	13	36	1.8	0.43 (0.18, 1.00)
Sindelar 1979a	1	80	9	88	0.5	0.12 (0.02, 0.94)
Sindelar 1979b	7	242	39	258	2.0	0.19 (0.09, 0.42)
Sindelar 1985	1	37	3	38	0.4	0.34 (0.04, 3.14)
Starr 2005	1	142	2	166	0.3	0.58 (0.05, 6.38)
Stokes 1977	11	55	21	62	2.5	0.59 (0.31, 1.11)
Valiance 1985	11	13	10	16	3.4	1.35 (0.87, 2.11)
Vinay 2019	9	90	7	90	1.6	1.29 (0.50, 3.30)
Walker 2013	1	31	3	36	0.4	0.39 (0.04, 3.53)
Walsh 1981	28	308	40	319	3.3	0.72 (0.46, 1.14)
Yildirim 2012	6	334	9	335	1.4	0.67 (0.24, 1.86)
Total (95% CI)		**10148**		**10349**	**100.0**	**0.70 (0.60, 0.80)**
Total events	665		974			

Heterogeneity: $\tau^2 = 0.11$; $\chi^2 = 103.58$, $df = 58$ ($p = 0.0002$): $I^2 = 44\%$
Test for overall effect: $Z = 4.91$ ($p < 0.00001$)

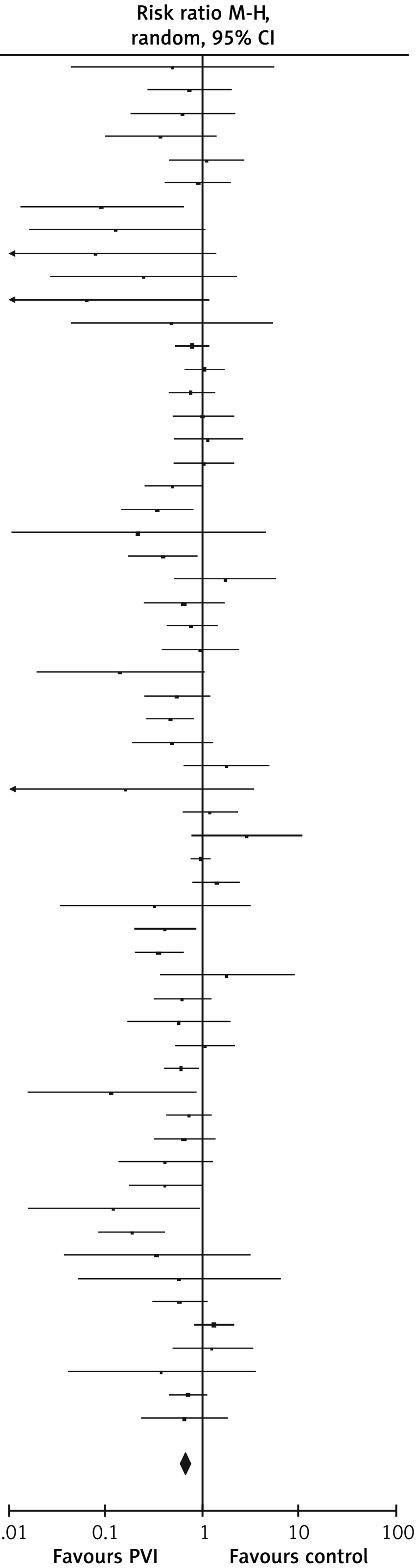

Figure 4. Forest plot of studies included in the meta-analysis (n = 59) using a random effects model. Risk ratios and 95% confidence intervals are shown

PVI – povidone iodine, control – saline or no treatment.

Study or subgroup	PVI Events	PVI Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, random, 95% CI
2.1.1. Saline						
Calkins 2019	1	223	8	234	0.4	0.13 (0.02, 1.04)
Chang 2006	0	120	6	124	0.2	0.08 (0.00, 1.40)
Cheng 2005	0	208	7	206	0.2	0.07 (0.00, 1.15)
Cohen 2020	1	77	2	76	0.3	0.49 (0.05, 5.33)
Galle 1980	9	31	9	36	2.0	1.16 (0.53, 2.56)
Ghafouri 2016	15	196	14	193	2.3	1.06 (0.52, 2.13)
Guzman 2002	7	80	4	80	1.1	1.75 (0.53, 5.75)
Harihara 2006	8	54	8	53	1.7	0.98 (0.40, 2.42)
Hassan 2016	1	50	14	100	0.5	0.14 (0.02, 1.06)
Johnson 1985	10	28	21	28	3.0	0.48 (0.28, 0.82)
Karuserci 2019	6	100	12	100	1.6	0.50 (0.20, 1.28)
Ko 1992	11	990	6	990	1.5	1.83 (0.68, 4.94)
Kokavec 2008	0	89	2	73	0.2	0.16 (0.01, 3.37)
Oestreicher 1989	16	267	15	273	2.4	1.09 (0.55, 2.16)
Pollock 1978	17	65	26	74	3.1	0.74 (0.45, 1.24)
Rogers 1983	4	86	11	101	1.3	0.43 (0.14, 1.29)
Sindelar 1979a	1	80	9	88	0.4	0.12 (0.02, 0.94)
Sindelar 1979b	7	242	39	258	2.0	0.19 (0.09, 0.42)
Sindelar 1985	1	37	3	38	0.4	0.34 (0.04, 3.14)
Valiance 1985	11	13	10	16	3.5	1.35 (0.87, 2.11)
Vinay 2019	9	90	7	90	1.6	1.29 (0.50, 3.30)
Walker 2013	1	31	3	36	0.4	0.39 (0.04, 3.53)
Subtotal (95% CI)		**3157**		**3267**	**30.3**	**0.65 (0.46, 0.92)**
Total events	136		236			
Heterogeneity: $\tau^2 = 0.33$; $\chi^2 = 52.52$, df = 21 ($p = 0.0002$); $I^2 = 60\%$						
Test for overall effect: $Z = 2.43$ ($p = 0.02$)						
2.1.2 No treatment						
Alobaidy 2020	1	200	2	200	0.3	0.50 (0.05, 5.47)
Anderson 2020	6	50	8	50	1.5	0.75 (0.28, 2.00)
Aref 2018	4	106	6	101	1.1	0.64 (0.18, 2.19)
Asad 2017	3	217	8	217	1.0	0.38 (0.10, 1.39)
Asghania 2011	10	284	9	284	1.7	1.11 (0.46, 2.69)
Barat 2016	12	200	13	200	2.1	0.92 (0.43, 1.97)
Barr 1978	1	28	23	60	0.5	0.09 (0.01, 0.66)
Charoenviboonphan 2011	1	299	4	300	0.4	0.25 (0.03, 2.23)
de Jong 1982	39	303	45	279	3.7	0.80 (0.54, 1.19)
Foster 1981	29	119	27	117	3.4	1.06 (0.67, 1.67)
Galland 1977	14	39	18	39	3.0	0.78 (0.45, 1.33)
Galland 1983	13	95	14	105	2.3	1.03 (0.51, 2.07)
Gilmore 1974	12	149	24	151	2.5	0.51 (0.26, 0.98)
Gilmore 1975	6	70	18	74	1.8	0.35 (0.15, 0.84)
Gilmore 1977	0	48	2	53	0.2	0.22 (0.01, 4.48)
Gray 1981	7	71	20	82	2.0	0.40 (0.18, 0.90)
Haas 2010	7	155	10	145	1.6	0.65 (0.26, 1.67)
Haider 2018	19	300	24	300	2.8	0.79 (0.44, 1.41)
lqbal 2015	9	83	16	83	2.1	0.56 (0.26, 1.20)
Kothius 1981	16	102	15	118	2.5	1.23 (0.64, 2.37)
Lau 1986	9	159	3	156	1.0	2.94 (0.81, 10.67)
Mahomed 2016	144	1520	147	1507	4.6	0.97 (0.78, 1.21)
McCluskey 1976	21	56	14	54	2.9	1.45 (0.82, 2.54)
Memon 2011	1	100	3	100	0.4	0.33 (0.04, 3.15)
Morgan 1978	10	166	22	154	2.3	0.42 (0.21, 0.86)
Morgan 1980	14	263	45	309	2.8	0.37 (0.21, 0.65)
Mwangi 2013	13	201	20	196	2.4	0.63 (0.32, 1.24)
Nandi 2015	4	136	7	138	1.1	0.58 (0.17, 1.94)
Olmez 2013	35	332	57	335	3.7	0.62 (0.42, 0.92)
Reid 2001	12	217	18	213	2.3	0.65 (0.32, 1.33)
Sherlock 1984	6	39	13	36	1.8	0.43 (0.18, 1.00)
Starr 2005	1	142	2	166	0.3	0.58 (0.05, 6.38)
Stokes 1977	11	55	21	62	2.6	0.59 (0.31, 1.11)
Walsh 1981	28	308	40	319	3.4	0.72 (0.46, 1.14)
Yildirim 2012	6	334	9	335	1.4	0.67 (0.24, 1.86)
Subtotal (95% CI)		**6946**		**7038**	**69.7**	**0.71 (0.61, 0.82)**
Total events	524		727			
Heterogeneity: $\tau^2 = 0.05$; $\chi^2 = 48.78$, df = 34 ($p = 0.05$); $I^2 = 30\%$						
Test for overall effect: $Z = 4.60$ ($p < 0.00001$)						
Total (95% CI)		**10103**		**10305**	**100.0**	**0.70 (0.61, 0.81)**
Total events	660		963			
Heterogeneity: $\tau^2 = 0.10$; $\chi^2 = 98.75$, df = 56 ($p = 0.0004$); $I^2 = 43\%$						
Test for overall effect: $Z = 4.90$ ($p < 0.00001$)						
Test for subgroup differences: $\chi^2 = 0.23$, df = 1 ($p = 0.63$); $I^2 = 0\%$						

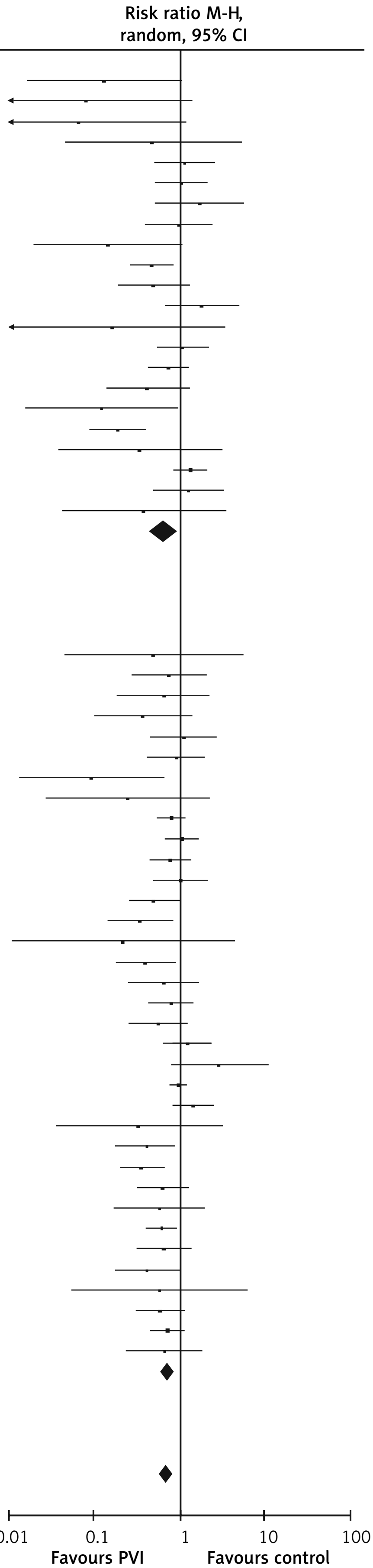

Figure 5. Forest plot for subgroup analysis of comparator type in studies using a random effects model. Risk ratios and 95% confidence intervals are shown

PVI – povidone iodine, control – saline or no treatment.

Study or subgroup	PVI Events	PVI Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, random, 95% CI
2.1.1 Irrigation						
Alobaidy 2020	1	200	2	200	0.3	0.50 (0.05, 5.47)
Anderson 2020	6	50	8	50	1.5	0.75 (0.28, 2.00)
Aref 2018	4	106	6	101	1.1	0.64 (0.18, 2.19)
Asad 2017	3	217	8	217	1.0	0.38 (0.10, 1.39)
Barat 2016	12	200	13	200	2.1	0.92 (0.43, 1.97)
Chang 2006	0	120	6	124	0.2	0.08 (0.00, 1.40)
Cheng 2005	0	208	7	206	0.2	0.07 (0.00, 1.15)
Cohen 2020	1	77	2	76	0.3	0.49 (0.05, 5.33)
de Jong 1982	39	303	45	279	3.6	0.80 (0.54, 1.19)
Galle 1980	9	31	9	36	2.0	1.16 (0.53, 2.56)
Ghafouri 2016	15	196	14	193	2.3	1.06 (0.52, 2.13)
Guzman 2002	7	80	4	80	1.2	1.75 (0.53, 5.75)
Haider 2018	19	300	24	300	2.8	0.79 (0.44, 1.41)
Harihara 2006	8	54	8	53	1.7	0.98 (0.40, 2.42)
Hassan 2016	1	50	14	100	0.5	0.14 (0.02, 1.06)
Iqbal 2015	9	83	16	83	2.1	0.56 (0.26, 1.20)
Johnson 1985	10	28	21	28	3.0	0.48 (0.28, 0.82)
Karuserci 2019	6	100	12	100	1.6	0.50 (0.20, 1.28)
Ko 1992	11	990	6	990	1.5	1.83 (0.68, 4.94)
Kokavec 2008	0	89	2	73	0.2	0.16 (0.01, 3.37)
Kothius 1981	16	102	15	118	2.5	1.23 (0.64, 2.37)
Lau 1986	9	159	3	156	1.0	2.94 (0.81, 10.67)
Mahomed 2016	144	1520	147	1507	4.5	0.97 (0.78, 1.21)
McCluskey 1976	21	56	14	54	2.9	1.45 (0.82, 2.54)
Muller 2018	4	23	2	21	0.7	1.83 (0.37, 8.96)
Mwangi 2013	13	201	20	196	2.4	0.63 (0.32, 1.24)
Oestreicher 1989	16	267	15	273	2.4	1.09 (0.55, 2.16)
Olmez 2013	35	332	57	335	3.7	0.62 (0.42, 0.92)
Rogers 1983	4	86	11	101	1.3	0.43 (0.14, 1.29)
Sindelar 1979a	1	80	9	88	0.5	0.12 (0.02, 0.94)
Sindelar 1979b	7	242	39	258	2.0	0.19 (0.09, 0.42)
Sindelar 1985	1	37	3	38	0.4	0.34 (0.04, 3.14)
Vinay 2019	9	90	7	90	1.6	1.29 (0.50, 3.30)
Yildirim 2012	6	334	9	335	1.4	0.67 (0.24, 1.86)
Subtotal (95 CI)		**7011**		**7059**	**56.6**	**0.77 (0.63, 0.93)**
Total events	447		578			
Heterogeneity: $\tau^2 = 0.11$; $\chi^2 = 58.65$, df = 33 (p = 0.004); I^2 = 44%						
Test for overall effect: Z = 2.68 (p = 0.007)						
2.1.2 Spray						
Foster 1981	29	119	27	117	3.3	1.06 (0.67, 1.67)
Galland 1977	14	39	18	39	3.0	0.78 (0.45, 1.33)
Galland 1983	13	95	14	105	2.3	1.03 (0.51, 2.07)
Gilmore 1974	12	149	24	151	2.5	0.51 (0.26, 0.98)
Gilmore 1975	6	70	18	74	1.8	0.35 (0.15, 0.84)
Gilmore 1977	0	48	2	53	0.2	0.22 (0.01, 4.48)
Gray 1981	7	71	20	82	2.0	0.40 (0.18, 0.90)
Morgan 1978	10	166	22	154	2.3	0.42 (0.21, 0.86)
Morgan 1980	14	263	45	309	2.8	0.37 (0.21, 0.65)
Pollock 1978	17	65	26	74	3.1	0.74 (0.45, 1.24)
Sherlock 1984	6	39	13	36	1.8	0.43 (0.18, 1.00)
Stokes 1977	11	55	21	62	2.6	0.59 (0.31, 1.11)
Walsh 1981	28	308	40	319	3.3	0.72 (0.46, 1.14)
Subtotal (95 CI)		**1487**		**1575**	**31.0**	**0.61 (0.49, 0.76)**
Total events	167		290			
Heterogeneity: $\tau^2 = 0.05$; $\chi^2 = 17.62$, df = 12 (p = 0.13); I^2 = 32%						
Test for overall effect: Z = 4.40 (p < 0.0001)						
2.1.3 Lavage						
Barr 1978	1	28	23	60	0.5	0.09 (0.01, 0.66)
Calkins 2019	1	223	8	234	0.5	0.13 (0.02, 1.04)
Parker 1985	1	22	9	23	0.5	0.12 (0.02, 0.84)
Valiance 1985	11	13	10	16	3.4	1.35 (0.87, 2.11)
Subtotal (95 CI)		**286**		**333**	**4.8**	**0.22 (0.02, 2.92)**
Total events	14		50			
Heterogeneity: $\tau^2 = 6.07$; $\chi^2 = 35.01$, df = 3 (p < 0.00001); I^2 = 91%						
Test for overall effect: Z = 1.14 (p = 0.25)						
2.1.4 Scrub						
Asghania 2011	10	284	9	284	1.8	1.11 (0.46, 2.69)
Haas 2010	7	155	10	145	1.6	0.65 (0.26, 1.67)
Memon 2011	1	100	3	100	0.4	0.33 (0.04, 3.15)
Nandi 2015	4	136	7	138	1.1	0.58 (0.17, 1.94)
Reid 2001	12	217	18	213	2.3	0.65 (0.32, 1.33)
Starr 2005	1	142	2	166	0.3	0.58 (0.05, 6.38)
Subtotal (95 CI)		**1034**		**1046**	**7.5**	**0.71 (0.46, 1.09)**
Total events	35		49			
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.63$, df = 5 (p = 0.90); I^2 = 0%						
Test for overall effect: Z = 1.58 (p = 0.11)						
Total (95 CI)		**9818**		**10013**	**100.0**	**0.70 (0.61, 0.81)**
Total events	663		967			
Heterogeneity: $\tau^2 = 0.11$; $\chi^2 = 102.17$, df = 56 (p = 0.0002); I^2 = 45%						
Test for overall effect Z = 4.80 (p < 0.00001)						
Test for subgroup differences: $\chi^2 = 3.11$, df = 3 (p = 0.38), I^2 = 3.5%						

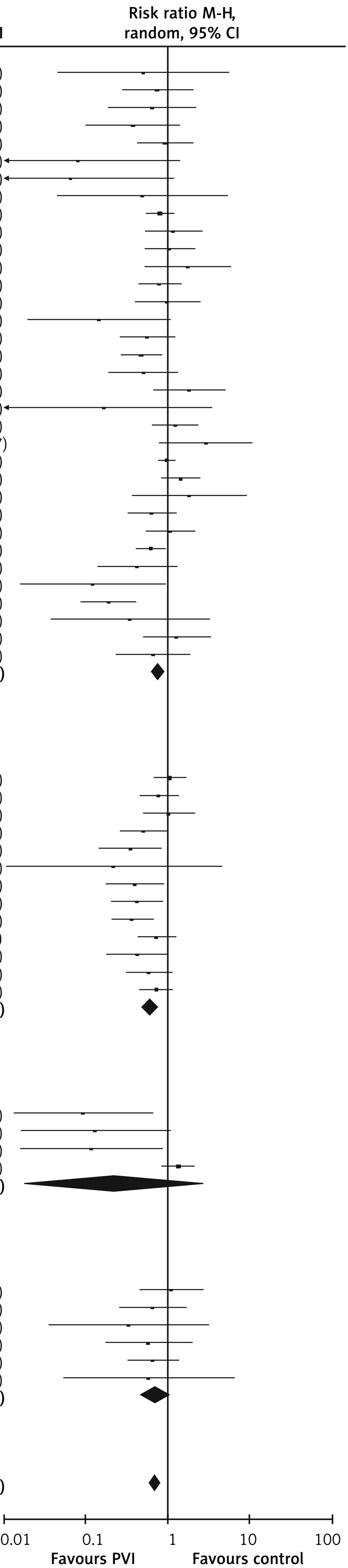

Figure 6. Forest plot for subgroup analysis of PVI application method in studies using a random effects model. Risk ratios and 95 confidence intervals are shown

PVI – povidone iodine, control – saline or no treatment.

Study or subgroup	PVI Events	PVI Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, random, 95% CI
4.1.2 Abdominal						
Anderson 2020	6	50	8	50	1.6	0.75 (0.28, 2.00)
Barr 1978	1	28	23	60	0.5	0.09 (0.01, 0.66)
de Jong 1982	39	303	45	279	4.5	0.90 (0.54, 1.19)
Foster 1981	29	119	27	117	4.0	1.06 (0.67, 1.67)
Galland 1977	14	39	18	39	3.5	0.78 (0.45, 1.33)
Galland 1983	13	95	14	105	2.6	1.03 (0.51, 2.07)
Gabe 1980	9	31	9	36	2.2	1.16 (0.53, 2.56)
Gilmore 1974	12	149	24	151	2.8	0.51 (0.26, 0.98)
Gilmore 1975	6	70	18	74	2.0	0.35 (0.15, 0.84)
Gray 1981	7	71	20	82	2.2	0.40 (0.18, 0.90)
Harihara 2006	8	54	8	53	1.8	0.98 (0.40, 2.42)
Iqbal 2015	9	83	16	83	2.4	0.56 (0.26, 1.20)
Karuserci 2019	6	100	12	100	1.7	0.50 (0.20, 1.28)
Kothius 1981	16	102	15	118	2.8	1.23 (0.64, 2.37)
Lau 1986	9	159	3	156	1.1	2.94 (0.81, 10.67)
McCluskey 1976	21	56	14	54	3.3	1.45 (0.82, 2.54)
Muller 2018	4	23	2	21	0.7	1.83 (0.37, 8.96)
Pollock 1978	17	65	26	74	3.6	0.74 (0.45, 1.24)
Rogers1983	4	86	11	101	1.4	0.43 (0.14, 1.29)
Sherlock 1984	6	39	13	36	2.0	0.43 (0.18, 1.00)
Sindelar 1979a	1	80	9	88	0.5	0.12 (0.02, 0.94)
Sindelar 1985	1	37	3	38	0.4	0.34 (0.04, 3.14)
Stokes 1977	11	55	21	62	2.9	0.59 (0.31, 1.11)
Valiance 1985	11	13	10	16	4.1	1.35 (0.87, 2.11)
Vinay 2019	9	90	7	90	1.7	1.29 (0.50, 3.30)
Walsh 1981	28	308	40	319	4.0	0.72 (0.46, 1.14)
Subtotal (95 CI)		**2305**		**2402**	**60.4**	**0.78 (0.64, 0.95)**
Total events	297		416			
Heterogeneity: $\tau^2 = 0.10$; $\chi^2 = 44.40$, $df = 25$ ($p = 0.010$); $I^2 = 44\%$						
Test for overall effect $Z = 2.49$ ($p = 0.01$)						
4.1.3 Gynaecological						
Alobaidy 2020	1	200	2	200	0.3	0.50 (0.05, 5.47)
Aref 2018	4	106	6	101	1.1	0.64 (0.18, 2.19)
Asad 2017	3	217	8	217	1.0	0.38 (0.10, 1.39)
Asghania 2011	10	284	9	284	1.9	1.11 (0.46, 2.69)
Barat 2016	12	200	13	200	2.3	0.92 (0.43, 1.97)
Charoenviboonphan 2011	1	299	4	300	0.4	0.25 (0.03, 2.23)
Guzman 2002	7	80	4	80	1.2	1.75 (0.53, 5.75)
Haas 2010	7	155	10	145	1.7	0.65 (0.26, 1.67)
Hassan 2016	1	50	14	100	0.5	0.14 (0.02, 1.06)
Mahomed 2016	144	1520	147	1507	5.8	0.97 (0.78, 1.21)
Memon 2011	1	100	3	100	0.4	0.33 (0.04, 3.15)
Mwangi 2013	13	201	20	196	2.7	0.63 (0.32, 1.24)
Nandi 2015	4	136	7	138	1.2	0.58 (0.17, 1.94)
Olmez 2013	35	332	57	335	4.5	0.62 (0.42, 0.92)
Reid 2001	12	217	18	213	2.6	0.65 (0.32, 1.33)
Starr 2005	1	142	2	166	0.3	0.58 (0.05, 6.38)
Yildirim 2012	6	334	9	335	1.5	0.67 (0.24, 1.86)
Subtotal (95 CI)		**4573**		**4617**	**29.7**	**0.81 (0.69, 0.95)**
Total events	262		333			
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 14.51$, $df = 16$ ($p = 0.56$); $I^2 = 0\%$						
Test for overall effect $Z = 2.62$ ($p = 0.009$)						
4.1.4 Orthopaedic						
Calkins 2019	1	223	8	234	0.5	0.13 (0.02, 1.04)
Kokavec 2008	0	89	2	73	0.2	0.16 (0.01, 3.37)
Subtotal (95 CI)		**312**		**307**	**0.7**	**0.14 (0.03, 0.78)**
Total events	1		10			
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.01$, $df = 1$ ($p = 0.90$); $I^2 = 0\%$						
Test for overall effect: $Z = 2.25$ ($p = 0.02$)						
4.1.5 Accident						
Ghafouri 2016	15	196	14	193	2.6	1.06 (0.52, 2.13)
Morgan 1978	10	166	22	154	2.5	0.42 (0.21, 0.86)
Morgan 1980	14	263	45	309	3.2	0.37 (0.21, 0.65)
Subtotal (95 CI)		**625**		**656**	**8.4**	**0.54 (0.28, 1.02)**
Total events	39		81			
Heterogeneity: $\tau^2 = 0.21$; $\chi^2 = 5.69$, $df = 2$ ($p = 0.06$); $I^2 = 65\%$						
Test for overall effect $Z = 1.89$ ($p = 0.06$)						
4.1.6 Spinal						
Chang 2006	0	120	6	124	0.2	0.08 (0.00, 1.40)
Cheng 2005	0	208	7	206	0.2	0.07 (0.00, 1.15)
Cohen 2020	1	77	2	76	0.3	0.49 (0.05, 5.33)
Subtotal (95 CI)		**405**		**406**	**0.8**	**0.16 (0.03, 0.76)**
Total events	1		15			
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.56$, $df = 2$ ($p = 0.46$); $I^2 = 0\%$						
Test for overall effect $Z = 2.31$ ($p = 0.02$)						
Total (95 CI)		**8220**		**8388**	**100.0**	**0.72 (0.63, 0.83)**
Total events	600		855			
Heterogeneity: $\tau^2 = 0.08$; $\chi^2 = 79.68$, $df = 50$ ($p = 0.005$); $I^2 = 37\%$						
Test for overall effect $Z = 4.43$ ($p < 0.00001$)						
Test for subgroup differences: $\chi^2 = 9.34$, $df = 4$ ($p = 0.05$), $I^2 = 57.2\%$						

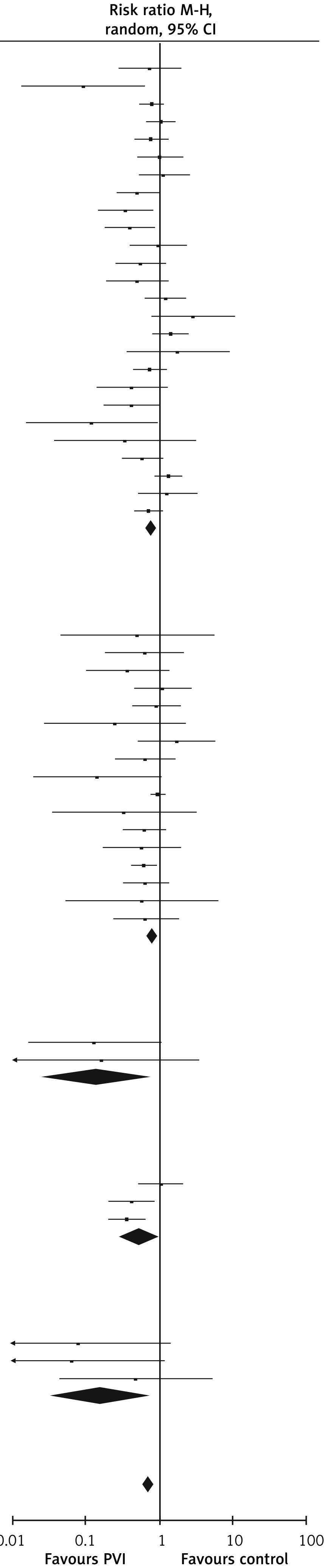

Figure 7. Forest plot for subgroup analysis of surgery category in studies using a random effects model. Risk ratios and 95 confidence intervals are shown

PVI – povidone iodine, control – saline or no treatment.

Study or subgroup	PVI Events	PVI Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, random, 95% CI
3.1.1 Elective						
Alobaidy 2020	1	200	2	200	0.3	0.50 (0.05, 5.47)
Aref 2018	4	106	6	101	1.0	0.64 (0.18, 2.19)
Asghania 2011	10	284	9	284	1.7	1.11 (0.46, 2.69)
Barat 2016	12	200	13	200	2.1	0.92 (0.43, 1.97)
Calkins 2019	1	223	8	234	0.4	0.13 (0.02, 1.04)
Chang 2006	0	120	6	124	0.2	0.08 (0.00, 1.40)
Cheng 2005	0	208	7	206	0.2	0.07 (0.00, 1.15)
Cohen 2020	1	77	2	76	0.3	0.49 (0.05, 5.33)
Gray 1981	7	71	20	82	1.9	0.40 (0.18, 0.90)
Guzman 2002	7	80	4	80	1.1	1.75 (0.53, 5.75)
Haas 2010	7	155	10	145	1.6	0.65 (0.26, 1.67)
Haider 2018	19	300	24	300	2.7	0.79 (0.44, 1.41)
Harihara 2006	8	54	8	53	1.7	0.98 (0.40, 2.42)
Hassan 2016	1	50	14	100	0.5	0.14 (0.02, 1.06)
Johnson 1985	10	28	21	28	2.9	0.48 (0.28, 0.82)
Kokavec 2008	0	89	2	73	0.2	0.16 (0.01, 3.37)
Kothius 1981	16	102	15	118	2.4	1.23 (0.64, 2.37)
Mahomed 2016	81	757	82	751	4.1	0.98 (0.73, 1.31)
Muller 2018	4	23	2	21	0.7	1.83 (0.37, 8.96)
Parker 1985	1	22	9	23	0.5	0.12 (0.02, 0.84)
Reid 2001	12	217	18	213	2.2	0.65 (0.32, 1.33)
Sindelar 1979a	1	80	9	88	0.4	0.12 (0.02, 0.94)
Starr 2005	1	142	2	166	0.3	0.58 (0.05, 6.38)
Vinay 2019	9	90	7	90	1.6	1.29 (0.50, 3.30)
Walker 2013	1	31	3	36	0.4	0.39 (0.04, 3.53)
Subtotal (95 CI)		**3709**		**3792**	**31.6**	**0.70 (0.55, 0.91)**
Total events	214		303			
Heterogeneity: $\tau^2 = 0.10$; $\chi^2 = 35.57$, $df = 24$ ($p = 0.06$); $I^2 = 33\%$						
Test for overall effect: $Z = 2.73$ ($p = 0.006$)						
3.1.2 Urgent						
Anderson 2020	6	50	8	50	1.5	0.75 (0.28, 2.00)
Asad 2017	3	217	8	217	1.0	0.38 (0.10, 1.39)
Foster 1981	29	119	27	117	3.3	1.06 (0.67, 1.67)
Galland 1983	13	95	14	105	2.3	1.03 (0.51, 2.07)
Ghafouri 2016	15	196	14	193	2.3	1.06 (0.52, 2.13)
Iqbal 2015	9	83	16	83	2.1	0.56 (0.26, 1.20)
Lau 1986	9	159	3	156	1.0	2.94 (0.81, 10.67)
Mahomed 2016	63	763	65	756	3.9	0.96 (0.69, 1.34)
Morgan 1978	10	166	22	154	2.2	0.42 (0.21, 0.86)
Morgan 1980	14	263	45	309	2.7	0.37 (0.21, 0.65)
Sherlock 1984	6	39	13	36	1.8	0.43 (0.18, 1.00)
Stokes 1977	11	55	21	62	2.5	0.59 (0.31, 1.11)
Subtotal (95 CI)		**2205**		**2238**	**26.4**	**0.72 (0.54, 0.95)**
Total events	188		256			
Heterogeneity: $\tau^2 = 0.12$; $\chi^2 = 22.61$, $df = 11$ ($p = 0.02$); $I^2 = 51\%$						
Test for overall effect: $Z = 2.31$ ($p = 0.02$)						
3.1.3 Mixed						
Barr 1978	1	28	23	60	0.5	0.09 (0.01, 0.66)
Charoenviboonphan 2011	1	299	4	300	0.4	0.25 (0.03, 2.23)
de Jong 1982	39	303	45	279	3.6	0.80 (0.54, 1.19)
Galland 1977	14	39	18	39	2.9	0.78 (0.45, 1.33)
Gilmore 1974	12	149	24	151	2.4	0.51 (0.26, 0.98)
Gilmore 1975	6	70	18	74	1.8	0.35 (0.15, 0.84)
Gilmore 1977	0	48	2	53	0.2	0.22 (0.01, 4.48)
Karuserci 2019	6	100	12	100	1.6	0.50 (0.20, 1.28)
Ko 1992	11	990	6	990	1.5	1.83 (0.68, 4.94)
McCluskey 1976	21	56	14	54	2.8	1.45 (0.82, 2.54)
Memon 2011	1	100	3	100	0.4	0.33 (0.04, 3.15)
Mwangi 2013	13	201	20	196	2.4	0.63 (0.32, 1.24)
Nandi 2015	4	136	7	138	1.1	0.58 (0.17, 1.94)
Oestreicher 1989	16	267	15	273	2.3	1.09 (0.55, 2.16)
Olmez 2013	35	332	57	335	3.6	0.62 (0.42, 0.92)
Pollock 1978	17	65	26	74	3.0	0.74 (0.45, 1.24)
Rogers1983	4	86	11	101	1.2	0.43 (0.14, 1.29)
Sindelar 1979	137	242	39	258	2.0	0.19 (0.09, 0.42)
Sindelar 1985	1	37	3	38	0.4	0.34 (0.04, 3.14)
Valiance 1985	11	13	10	16	3.3	1.35 (0.87, 2.11)
Walsh 1981	28	308	40	319	3.3	0.72 (0.46, 1.14)
Yildirim 2012	6	334	9	335	1.4	0.67 (0.24, 1.86)
Subtotal (95 CI)		**4203**		**4283**	**42.0**	**0.67 (0.53, 0.85)**
Total events	254		406			
Heterogeneity: $\tau^2 = 0.14$; $\chi^2 = 44.85$, $df = 21$ ($p = 0.002$); $I^2 = 53\%$						
Test for overall effect: $Z = 3.27$ ($p = 0.001$)						
Total (95 CI)		**10117**		**10313**	**100.0**	**0.70 (0.61, 0.80)**
Total events	656		965			
Heterogeneity: $\tau^2 = 0.11$; $\chi^2 = 102.44$, $df = 58$ ($p = 0.0003$); $I^2 = 43\%$						
Test for overall effect: $Z = 4.95$ ($p < 0.00001$)						
Test for subgroup differences: $\chi^2 = 0.12$, $df = 2$ ($p = 0.94$), $I^2 = 0\%$						

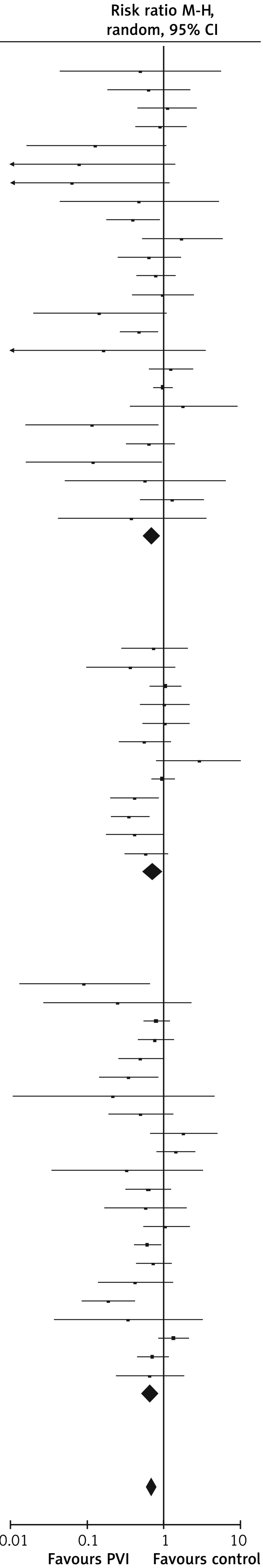

Figure 8. Forest plot for subgroup analysis of type of procedure in studies using a random effects model. Risk ratios and 95 confidence intervals are shown

PVI – povidone iodine, control – saline or no treatment.

dated and uniform definition of SSI, are needed to validate these findings.

Review criteria: how did you gather, select and analyze the information you considered in your review?

A systematic literature search was conducted of MEDLINE (PubMed) and Cochrane Register of Controlled Trials (CENTRAL) in June 2021. No time limit was applied as several studies were published earlier than 1990. The following search terms were used in various combinations: surgical site infection, wound infection, SSI, post-operative, povidone-iodine, betadine, irrigation, and spray, and lavage, intraoperative and anti-infective agents.

Conflict of interest

The authors declare no conflict of interest.

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